WHAT IS CLAIMED IS:

1. A transgenic nonhuman mammal comprising two human immunoglobulin loci, wherein one of two said human immunoglobulin loci is a human heavy chain locus and the other locus is a human light chain locus; and

wherein only one of said loci is of a transchromosome.

2. The transgenic nonhuman mammal of claim 1, wherein the transchromosome is autonomous.

3. The transgenic nonhuman mammal of claim 1, wherein the human light chain locus is associated with an endogenous mammalian chromosome.

4. The transgenic nonhuman mammal of claim 1, wherein the human heavy chain locus is of a transchromosome and the human light chain locus is associated with an endogenous mammalian chromosome.

5. The transgenic nonhuman mammal of claim 1, wherein the human light chain locus is of a transchromosome and the human heavy chain locus is associated with an endogenous mammalian chromosome.

6. The transgenic nonhuman mammal of claim 1, wherein the endogenous mammalian heavy chain locus and at least one mammalian light chain locus are inactivated.

7. The transgenic nonhuman mammal of claim 6, wherein the endogenous mammalian heavy chain locus and kappa light chain locus are inactivated.

8. The transgenic nonhuman mammal of claim 4, wherein at least a part of the human light chain locus is cloned into a YAC vector.

9. The transgenic nonhuman mammal of claim 1, wherein the transgenic nonhuman mammal is a mouse.

10. The transgenic nonhuman mammal of claim 1, wherein the transchromosome comprises a fragment of human chromosome 14.

11. The transgenic nonhuman mammal of claim 1, wherein the human heavy chain locus is comprised in hCF(SC20) and the human light chain locus is comprised in the human kappa light chain locus transgene KCo5.

12. A method for generating a plurality of B cells expressing human antibody sequences, the method comprising:

providing the transgenic nonhuman mammal of claim 1; and

immunizing the transgenic nonhuman mammal to generate a plurality of B cells expressing human antibody sequences.

13. The method of claim 12, further comprising collecting the plurality of B cells expressing sequences expressing human antibodies.

14. The method of claim 13, further comprising fusing the plurality of B cells with immortalized cells to form hybridomas.

15. The method of claim 14, further comprising collecting the human antibody sequences from the hybridomas.

16. The method of claim 15, wherein the human antibody sequences are purified.

17. The method of claim 12, further comprising collecting the sequences encoding human antibodies.

18. The method of claim 17, wherein the sequences encoding human antibodies are full length.

19. The method of claim 18, further comprising expressing the sequences in a transfected cell.

20. The method of claim 12, wherein the transchromosome is a fragment of human chromosome 14.

21. The method of claim 12, wherein the human transchromosome is hCF(SC20).

22. The method of claim 12, wherein the human light chain locus comprises unrearranged sequences from the natural human kappa light chain locus.

23. The method of claim 12, wherein the human kappa light chain locus is the inserted KCo5 transgene.

24. The method of claim 12, wherein the plurality of B cells comprises at least a first B cell encoding an antibody with a first isotype selected from the group consisting of IgA, IgD, IgE, IgG and IgM.

25. The method of claim 24, wherein the plurality of B cells further comprises at least a second B cell encoding an antibody with a second isotype different from the first isotype selected from the group consisting of IgA, IgD, IgE, IgG and IgM.

26. The method of claim 12, wherein the plurality of B cells comprise at least five B cells each encoding an antibody having a different isotype wherein the isotypes of the antibodies are IgA, IgD, IgE, IgG and IgM respectively.

27. The method of claim 24, wherein the IgA isotype is IgA_1 or IgA_2.

28. The method of claim 24, wherein the IgG isotype is IgG_1, IgG_2, IgG_3 or IgG_4.

29. A method for generating a human sequence antibody that binds to a predetermined antigen, the method comprising the following steps:

immunizing the transgenic nonhuman mammal of claim 1 with the predetermined antigen; and

collecting the human sequence antibody from the immunized transgenic nonhuman mammal.

30. The method of claim 29, wherein the human sequence antibody binds to a predetermined antigen with an equilibrium association constant (K_a) of at least 10^{10} M^{-1}.

31. The method of claim 29, wherein the human sequence antibody binds to a predetermined antigen with an equilibrium association constant (K_a) of at least 10^9 M^{-1}.

32. The method of claim 29, wherein the human sequence antibody binds to a predetermined antigen with an equilibrium association constant (K_a) of at least 10^8 M^{-1}.

33. The method of claim 29, wherein the human sequence antibodies are monoclonal.

34. The method of claim 29, wherein the human sequence antibody is a $F(ab')_2$, Fab, F_v, or F_d fragment.

35. The method of claim 29, wherein the human sequence antibody is antigen-specific.

36. A method for generating antigen-specific hybridomas secreting human sequence antibody, the method comprising:

immunizing the transgenic nonhuman mammal of claim 1 with a predetermined antigen;

fusing lymphocytes from the transgenic nonhuman mammal with immortalized cells to form hybridoma cells; and

determining the binding of the antibody produced by the hybridoma cells to the predetermined antigen.

37. The method of claim 36, wherein greater than 50% of the antigen-specific hybridoma clones secrete antibody having human heavy chain and human light chain.

38. A method for generating a human sequence antibody that binds to a predetermined antigen, the method comprising the following steps:

immunizing the transgenic nonhuman mammal of claim 1 with the predetermined antigen; and

screening hybridoma cells formed for the presence of antigen reactive antibodies.

39. The method of claim 38, wherein the hybridoma cells are subcloned at an efficiency of greater than 20%.

40. The method of claim 38, wherein the antigen reactive antibodies are secreted from the hybridoma in culture.

41. The method of claim 38, wherein the antigen reactive antibodies are substantially pure.

42. The method of claim 41, wherein the substantially pure antibodies are formulated for therapeutic use.

43. A method for producing rearranged immunoglobulin sequences comprising:

providing the transgenic nonhuman mammal of claim 1, and

obtaining the rearranged immunoglobulin sequences from the transgenic nonhuman mammal.

44. The method of claim 43, wherein the obtaining step comprises collecting B cell lymphocytes containing the rearranged immunoglobulin sequences from the transgenic nonhuman mammal.

45. The method of claim 43, wherein the obtaining step comprises isolating and amplifying mRNA from B cell lymphocytes to generate cDNA.

46. The method of claim 45, further comprising isolating and amplifying heavy and light chain variable region sequences from the cDNA.

47. An isolated nucleic acid encoding the heavy and light chain variable region sequences of claim 46.

48. An isolated nucleic acid encoding the heavy chain variable region sequences of claim 46.

49. An isolated nucleic acid encoding the light chain variable region sequences of claim 46.

50. A vector comprising the nucleic acid of claim 47.

51. An expression vector comprising the nucleic acid of claim 47 in which the heavy and light chain variable regions sequences of the nucleic acid are operatively linked with a regulatory sequence that controls expression of the nucleic acid in a host cell.

52. A host cell comprising the nucleic acid of claim 47, or progeny of the cell.

53. The host cell of claim 52 which is a eukaryote.

54. The method of claim 43, further comprising:

culturing the host cell of claim 52 under conditions such that the nucleic acid is expressed; and

recovering the nucleic acid from the cultured host cell or its cultured medium.

55. A method of producing a human antibody display library, the method comprising:

introducing an immunogen into the transgenic nonhuman mammal of claim 1;

isolating a population of nucleic acids encoding human antibody chains from lymphatic cells of the nonhuman transgenic animal; and

forming a library of display packages displaying the antibody chains, wherein a library member comprises a nucleic acid encoding an antibody chain, and the antibody chain is displayed from the package.

56. The method of claim 55 wherein the nonhuman transgenic mammal lacks a detectable titer to the immunogen when the isolating step is performed.

57. The method of claim 55, wherein the immunogen is a nucleic acid.

58. The method of claim 55, wherein the nucleic acid encodes a membrane bound receptor.

59. A method for generating a human sequence antibody, or fragment thereof, that binds to a predetermined antigen, the method comprising the following steps:

immunizing the transgenic nonhuman mammal of claim 1 with the predetermined antigen;

collecting antibody V region sequences from the immunized transgenic nonhuman mammal;

cloning the collected V regions into a DNA vector generating an expression library; and

expressing the library to identify V region sequences that encode an antibody, or fragment thereof, that binds to the predetermined antigen.

60. A method for generating a human sequence antibody or fragment thereof, that binds to a predetermined antigen, the method comprising the following steps:

immunizing the transgenic nonhuman mammal of claim 1 with the predetermined antigen;

isolating cDNA coding at least one human antibody V region from B cells of the immunized transgenic nonhuman mammal or from hybridomas generated by fusion of said B cell and an immortalized cell;

cloning said cDNA into an expression vector;

introducing said vector into a host cell;

culturing said host cell; and

collecting said human sequence antibody or fragment thereof from said host cell or culture medium thereof.

61. The method of claim 60, wherein the isolating step is performed by PCR.

62. The method of claim 60, wherein the isolating step is performed by cDNA library screening using at least one DNA probe.

63. The method of claim 60, wherein the isolating step is performed by phage display library screening.

64. The method of claim 60, wherein the cDNA encodes full length human antibody sequences.

65. The method of claim 60, wherein the collected human sequence antibody isotype is different from the isotype of antibody producing cells of said immunized transgenic nonhuman mammal.

66. A method of improving the stability of a transchromosomic mouse hybridoma cell expressing a human antibody reactive with a predetermined antigen, the method comprising:

breeding a first mouse, the first mouse comprising a first human immunoglobulin locus on a transchromosome, together with a second mouse, the second mouse comprising a second human immunoglobulin locus inserted within an endogenous mouse chromosome;

obtaining a third mouse from the breeding, the third mouse comprising both the first and the second human immunoglobulin loci;

immunizing the third mouse, or its progeny, with the predetermined antigen;

collecting B cells from the immunized mouse; and

fusing the B cells with immortalized cells to obtain hybridoma cells expressing the human antibody reactive with the predetermined antigen.

67. The method of claim 66 further comprising:

culturing the hybridoma cells in media;

testing the media to identify the presence of hybridoma cells that express human antibodies reactive with the predetermined antigen;

diluting the hybridoma cells; and

culturing the diluted hybridoma cells to obtain clonal cell lines expressing a monoclonal human antibody reactive with the predetermined antigen.

68. The method of claim 67 wherein the clonal cell lines are obtained from at least 50% of the identified hybridoma cells.

69. A mouse hybridoma cell secreting a human sequence antibody having an IgA isotype that binds to a specified antigen with an equilibrium association constant (K_a) of at least 10^{10} M^{-1}.

70. A human sequence antibody having an IgA isotype that binds to a specified antigen with an equilibrium association constant (K_a) of at least 10^{10} M^{-1}.

71. The transgenic nonhuman mammal of claim 1, further comprising a mutation of a gene, wherein the mutation increases the immune response to autoantigen.

72. The transgenic nonhuman mammal of claim 71, wherein the mutation is the inactivation of the Fc-gamma IIB gene.

73. The method of claim 12, further comprising a mutation of a gene, wherein the mutation increases the immune response to autoantigen.

74. The method of claim 73, wherein the mutation is the inactivation of the Fc-gamma IIB gene.

75. The method of claim 29, further comprising a mutation of a gene, wherein the mutation increases the immune response to autoantigen.

76. The method of claim 75, wherein the mutation is the inactivation of the Fc-gamma IIB gene.

77. The method of claim 36, further comprising a mutation of a gene, wherein the mutation increases the immune response to autoantigen.

78. The method of claim 77, wherein the mutation is the inactivation of the Fc-gamma IIB gene.

79. The method of claim 38, further comprising a mutation of a gene, wherein the mutation increases the immune response to autoantigen.

80. The method of claim 79, wherein the mutation is the inactivation of the Fc-gamma IIB gene.

81. The method of claim 43, further comprising a mutation of a gene, wherein the mutation increases the immune response to autoantigen.

82. The method of claim 81, wherein the mutation is the inactivation of the Fc-gamma IIB gene.

83. The method of claim 55, further comprising a mutation of a gene, wherein the mutation increases the immune response to autoantigen.

84. The method of claim 83, wherein the mutation is the inactivation of the Fc-gamma IIB gene.

85. The method of claim 59, further comprising a mutation of a gene, wherein the mutation increases the immune response to autoantigen.

86. The method of claim 85, wherein the mutation is the inactivation of the Fc-gamma IIB gene.

87. The method of claim 60, further comprising a mutation of a gene, wherein the mutation increases the immune response to autoantigen.

88. The method of claim 87, wherein the mutation is the inactivation of the Fc-gamma IIB gene.